UNIVERSITY OF SPLIT
SCHOOL OF MEDICINE

ANDRIJA JUKIĆ

CROATIAN TRANSLATION AND VALIDATION OF THE SARCOPENIA QUALITY OF LIFE QUESTIONNAIRE

Diploma thesis

Academic year:
2017/2018

Mentor:

Assist. Prof. Mislav Radić, MD, PhD

Split, July 2018

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This diploma thesis is dedicated to my mother, Željana, who has always been there for me. In good times and in bad times.

1.INTRODUCTION

1.1. Definition

Sarcopenia is an age-related syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength. It contributes to the risk of physical frailty, functional impairment in older people, poor health-related quality of life and premature death (1). The term is from Greek σάρξ sarx, "flesh" and πενία penia, "poverty".

1.2. Classification

The Aging in Motion Coalition (AIM) has announced that the Centers for Disease Control and Prevention has established an ICD-10-CM code for sarcopenia, so that it can be recognized for separate reporting and data collection. The code, M62.84, has been available for use by the medical community since October 1, 2016 (2).

Sarcopenia can be considered ‘primary’ (or age-related) when no other cause is evident but ageing itself, while sarcopenia can be considered ‘secondary’ when one or more other causes are evident (Table 1) (3).

Table 1. Sarcopenia categories by cause

Primary sarcopenia	
Age related sarcopenia	No other cause except ageing
Secondary sarcopenia	
Activity related sarcopenia	Can result from bed rest, sedentary lifestyle, deconditioning or zero gravity conditions
Disease related sarcopenia	Associated with advanced organ failure, inflammatory disease, malignancy or endocrine disease
Nutrition related sarcopenia	Results from inadequate dietary intake of energy and/or protein, as with malabsorption, gastrointestinal disorders or use of medications that cause anorexia

European Working Group on Sarcopenia in Older People (EWGSOP) suggests a conceptual staging as ‘presarcopenia’, ‘sarcopenia’ and ‘severe sarcopenia’.

The ‘presarcopenia’ stage is characterised by low muscle mass without impact on muscle strength or physical performance. This stage can only be identified by techniques that measure muscle mass accurately and in reference to standard populations. The ‘sarcopenia’ stage is characterised by low muscle mass, plus low muscle strength or low physical performance. ‘Severe sarcopenia’ is the stage identified when all three criteria of the definition are met (low muscle mass, low muscle strength and low physical performance). Recognising stages of sarcopenia may help in selecting treatments and setting appropriate recovery goals (3).

Table 2. Stages of sarcopenia

Stage	Muscle mass	Muscle strength		Performance
Presarcopenia	↓			
Sarcopenia	↓	↓	or	↓
Severe sarcopenia	↓	↓		↓

1.3. Epidemiology

In order to estimate the prevalence of low muscle mass, sufficiently large samples of the general population are required. Techniques for assessing muscle mass in such settings include anthropometry, bioelectrical impedance (BIA) and dual energy x-ray absorptiometry (DXA). Anthropometric measures can appear to have certain errors in older people (4) .

BIA produces estimates of total fat mass and non-fat mass and has the advantage over DXA because of the fact that the equipment used is portable. However it is questioned to what extent BIA provides additional information beyond that from anthropometric measurements. DXA is able to divide total body mass into estimates of fat mass, bone mass and lean mass (which includes muscle tissue and solid organs). DXA has the advantage that its estimates can be restricted to an area of the body, such as the arms and legs and hence avoid measuring the lean mass of the solid organs. Cut-points for DXA have typically come from young adult values, specifically two standard deviations (SDs) below the sex-specific young adult mean

appendicular lean mass (ALM) divided by height squared. Example cut-points are 7.23 kg / m2 in males and 5.67 kg / m2 in females. Applying these cut-points to older populations gives estimates of prevalence such as of 20% of those aged 70-79 and 30% of those aged over 80.

Several measures exist for the measurement of muscle strength. Grip strength has been recommended as the most practical method of measuring muscle strength in the clinical setting and has been found to correlate physical performance measures in the lower limbs (Table 3) (3). Data from the inCHIANTI have been used to produce grip strength cut-points two standard deviations below a gender-specific young adult mean, showing a high prevalence of weak grip at age 65-74 (5). The most commonly described measure of physical performance in the assessment of sarcopenia is gait speed. Gait speed can be assessed in the clinical setting by measuring the time taken to walk a set distance, for example 4 m, at usual pace (4).

Table 3. Criteria for different study groups

	Criteria		
	Muscle group	**Muscle stregth**	**Physical performance**
ESPEN special interest groups	Percentage of muscle mass >2 SDs below mean in individuals aged 18-39 years in NHANES III cohort	X	Walking speed <0.8 m/s in the 4-min test or reduced performance in any functional test used for the comprehensive geriatric assessment
European working group on sarcopenia in older people	ALM/h2 Men ≤ 7.23 kg/m2 Women ≤ 5.67 kg/m2	Grip strength Men <30 kg Women <20 kg	Gait speed <0.8 m/s
International working group on sarcopenia	ALM Men ≤ 7.23 kg/m2 Women ≤ 5.67 kg/m2	X	Gait speed ≤1 m/s
Society of sarcopenia, cachexia and wasting disorders	ALM/h2 of >2 SDs below the mean of healthy persons aged between 20 and 30 years of the same ethnic group	X	Gait speed ≤1 m/s or walking distance <400 m during a 6-min walk
Foundation of NIH sarcopenia project	ALM Men <0.789 Women <0.512	Grip strength Men <26 kg Women <16 kg	X

Both men and women lose strength, with men losing almost twice as much strength as women. The loss of lean mass, as well as higher baseline strength, lower baseline leg lean mass, and older age, was independently associated with strength decline in both men and women (6). Estimates of the prevalence of gait speed below 0.8 m/s vary. A Spanish study found that 56% of men and women aged 75 and over fell below this level (4). Data from the Boston Area Community Health and Bone Survey showed higher lean mass index in black ($p = 0.001$) and Hispanic ($p = 0.06$) men when compared with white men after adjustment for confounding influences (7). In the Health ABC Study muscle strength was lower in black men and women compared to white men and women, despite the higher measures of lean mass observed in these groups. Black participants experienced greater declines in muscle strength when compared to white participants ($p = 0.001$) (6).

Auyeung *et al.* observed a decline in grip strength in Chinese participants that was more rapid than that of ASM and gait speed (8). Over a 2-year period, women experienced a 10.0% decline, while men experienced a 3.85% decline. When compared to other ethnic populations, the rate of decline in muscle strength was much more rapid in Asian populations (9). Rates of decline in physical functioning appear to follow a similar pattern as those described for muscle strength with the most rapid declines being experienced among Asian populations and the most gradual declines shown in white populations (8, 10).

1.4. Etiology

Multiple factors are associated with decreased muscle mass and/or strength in older adults. We can divide these factors into primary and secondary (Table 4) (11):

Table 4. Primary and Secondary types of Sarcopenia

Primary	Age related: sex hormones, muscle apoptosis, mitochondrial dysfunction
Secondary	Activity related: physical inactivity, disuse, decon ditioning, zero gravity
	Nutrition related: inadequate dietary intake, malabsorption, gastrointestinal disorders or medications that cause anorexia
	Endocrine disorder related: obesity, insulin resistance, inflammatory cytokine, steroid treatment, abnormal thyroid function
	Neurodegenerative disorder related: stroke, parkinsonism, diabetic neuropathy
	Chronic disease related: malignancy, advanced organ failure

The loss of muscle mass and strength is related to the progressive atrophy and loss of individual muscle fibres associated with the loss of motor units, and a concomitant reduction in muscle 'quality' due to the infiltration of fat and other non-contractile material. These age-related changes in skeletal muscle can be largely attributed to the complex interaction of factors that affect neuromuscular transmission, muscle architecture, fibre composition, excitation–contraction coupling, and metabolism (12).

Changes in the hormonal and inflammatory settings result in impairment of protein synthesis and increased protein degradation. Buildup or ROS (reactive oxygen species) may result in mitochondrial dysfunction which impairs muscle respiration and may result in fiber deterioration through loss of myonuclei. Changes in expressing myogenic regulatory factors may impair the ability of aged muscle to repair damage (13).

It has been stated that alterations may result in a decline in the content and rate of production of ATP, which may affect tissue function, contribute to the aging process, and also lead to several disease states. With aging, ATP content and production decreased by approximately 50% in isolated rat mitochondria from the gastrocnemius muscle. However, no decline was observed in heart mitochondria. The decline observed in skeletal muscle may be a factor in the process of sarcopenia, which increases in incidence with advancing age (14).

In 2004, Larsson and colleagues published the first experimental evidence providing a causative link between mtDNA mutations and mammalian aging. They demonstrated that mtDNA mutations and deletions are responsible for a progressive decline in respiratory function of mitochondrially encoded complexes, that was evident as early as 12 weeks, resulting in decreased oxygen consumption and ATP production (15).

1.5. Pathology

Neuron loss is a progressive, irreversible process that increases with age. Age-related neurodegeneration may contribute importantly to the effects of age on muscle. Multiple levels of the nervous system are affected by age, including the motor cortex, the spinal cord, peripheral neurons, and the neuromuscular junction. Testosterone concentrations decline as age increase, suggesting that low plasma testosterone levels can cause or accelerate muscle- and age-related diseases, as sarcopenia (5).

Sarcopenia induces a change in the proportion of skeletal muscle fibers, inducing a shift from type II (fast) to type I (slow) fibers as well as preferential loss of type II fibers (16).

Higher levels of inflammatory markers were generally associated with greater 5-year decline in thigh muscle area. Most associations, with the exception of soluble receptors, were attenuated by adjustment for 5-year change in weight. Higher TNF-alpha and interleukin-6 soluble receptor levels remained associated with greater decline in grip strength in men. Analyses in a subgroup of weight-stable persons showed that higher levels of TNF-alpha and its soluble receptors were associated with 5-year decline in thigh muscle area and that higher levels of TNF-alpha were associated with decline in grip strength (17).

In recent years, it became evident that in these two muscle wasting disorders specific regulating molecules are increased in expression (e.g. members of the ubiquitin-proteasome system, myostatin, apoptosis inducing factors), whereas other factors (e.g. insulin-like growth factor 1) are down-regulated (18).

1.6. Clinical findings

Beginning as early as the 4th decade of life, evidence suggests that skeletal muscle mass and skeletal muscle strength decline in a linear fashion, with up to 50% of mass being lost by the 8th decade of life (19).

It is usually accompanied by physical inactivity, decreased mobility, slow gait and poor physical endurance which are also common features of the frailty syndrome.

Moreover, aging and physical disability are also related to an increase in fat mass, particularly visceral fat, which is an important factor in the development of metabolic syndrome and cardiovascular disease (CVD). Therefore, sarcopenia with obesity in the elderly may synergistically increase their effect on metabolic disorders, CVD and mortality as well as physical disability (5).

Sarcopenia represents a major risk factor for adverse events associated with frailty, weakness, falls, immobility, functional decline, and institutionalization. Testosterone is the

main anabolic hormone for protein synthesis in skeletal muscle and has been shown to promote muscle regeneration via satellite cell activation. Serum testosterone levels decline with age in both men and women, and this decline is associated with decreased muscle mass and strength, especially in men. Similarly, in females, menopause is associated with a marked reduction in estrogen levels and an accelerated decline in muscle mass and strength (20).

Vitamin D reduction has been another clinical finding that was noticed in patients with sarcopenia. Even though it is still unclear what effect does vitamin D have on skeletal muscles, it has been shown that its supplements, when given to vitamin D deficient patients, resulted in improved muscle strength ability and a reduction in falls and fractures (5).

Insulin decreases protein degradation and stimulates protein synthesis. An increase in insulin resistance with age could result in inhibition of the nitric oxide cascade which would result in a lower absorption of amino acids for protein synthesis (20). Diabetes mellitus is a condition that is frequently associated with sarcopenia in the elderly. It promotes the reduction in muscle mass and strength through hyperglycemia, obesity, and increased general inflammation, all of which are known risk factors for sarcopenia (11).

1.7. Differential diagnosis

Sarcopenia can also be featured in some other syndromes associated with muscle waisting. Cachexia has recently been defined as a complex metabolic syndrome associated with underlying illness and characterised by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders). Anorexia, inflammation, insulin resistance and increased muscle protein breakdown are frequently associated with cachexia (21).

Frailty and sarcopenia overlap. Most frail older people exhibit sarcopenia and some older people with sarcopenia are also frail. The general concept of frailty, however, goes beyond physical factors to encompass psychological and social dimensions as well, including cognitive status, social support and other environmental factors (22).

In conditions such as malignancy, rheumatoid arthritis and ageing, lean body mass is lost while fat mass may be preserved or even increased. This state is called sarcopenic obesity, and thus the relationship between age-related reduction of muscle mass and strength is often independent of body mass (23).

1.8. Treatment

Physical activity can be seen as an important factor to reverse or modify the development of this condition. Several treatments have been proposed for the treatment of this loss of muscle and strength, but there is no doubt that exercise represents the most important approach to prevent and treat sarcopenia. There are four types of exercise recommended for older adults: aerobic, progressive resistance, flexibility and balance training (24).

Aerobic exercise is a form of structured physical activity characterized by rhythmic and repetitive movements of large muscles, for sustained periods that depends primarily on the use of oxygen to meet energy demands through aerobic metabolism. Examples for this type of exercise are jogging, swimming, tennis, aerobics, bicycle riding and so on. Progressive resistance exercise requires muscles to generate force to move or resist weight, with increase in intensity as physical capacity improves. It relies on anaerobic metabolism to meet energy demands. Examples are lifting weights, working with resistance bands, pull ups, push ups, sit ups and so on. Several studies have shown that, even in elderly, progressive resistance exercises increases muscle mass, muscle strength, and muscle power. It can attenuate sarcopenia in several ways, such as: improving muscle size and function, reducing balance and flexibility problems, and reducing the development of many sarcopenia related comorbidities. Its successfulness depends on several factors (intensity, training volume, periods of recovery between sets, and frequency of training) (24).

Flexibility exercise is a possibility to move a joint through a whole range of motion. Stretches can be static (choose a position, hold stretch, than relax), dynamic (fluid motion, example is Tai Chi), active (yoga) or a combination. Balance training is an exercise that focuses on helping to maintain stability during daily activities and other exercises, preventing falls. It can be static (such as standing on one leg) or dynamic (such as walking a tightrope), with hand support as needed. Examples of balance training include tandem walking, standing

on heels or toes, walking on compliant surface such as foam matresses, walking backwards etc. (24).

After injury, the quiescent stem cells that reside between the basal lamina and sarcolemma are activated, proliferate, and replenish the satellite cell pool or fuse and differentiate to form multinucleated myofibers. However, little success has been achieved by exogenous stem cell delivery. Still, certain stem-cell-based strategies for myofiber regeneration have been described (Table 5) (20).

Table 5. Stem-cell-based strategies for myofiber regeneration

Cell type	**Description**	**Progress towards therapeutic potential**	**Challenges**
Satellite cells	Adult stem cells; Express Pax7 transcription factor; Necessary for proliferation and maintenance of muscle stem cell pool	50 years from first identification to pure cell isolation; Surface markers identified for satellite cell isolation are not necessarily reflected in human physiology; Need for optimized isolation and more efficient expansion	Very difficult to isolate and expand in culture; Limited engrafment efficiency.
Muscle derived stem cells	Adult stem cells; Identified in the interstitial space in mice; Nonadherent cell population	Improve muscle regeneration; Can expand in vitro up to 30 passages while retaining myogenic capacity	Poor engraftment efficiency; No functional improvement despite histological improvement.
Perivascular stem cells	Adult stem cells; Found in muscle microvasculature typically vessel associated CD146+/NG2+/ALP+; Express satellite cell markers; Assume satellite cell position after injection	Currently ongoing phase I/II clinical trial for pediatric muscular dystrophy; Can be cultured up to 20 passages while retaining myogenic capacity; Better engraftment efficiency than satellite cells; Improve muscle function	Varaible in vitro scalability gives them a finite culture life span

Embryonic stem cells	Pluripotent cells isolated from inner cell mass of blastocyst	Generation of large quantities in vitro is possible; Engraftment ability has been demonstrated in murine models	Difficult to recapitulate the skeletal muscle lineage in vitro; Potential immunologic mismatch; Ethical concerns
Induced pluripotent stem cells (iPSC)	Genetically reprogrammed somatic cells inducing a pluripotent state	Generation of Pax7 + iPSCs is possible; Genertion of functional, human skeletal myogenic progenitors has been accomplished; Promote skeletal muscle regeneration and functional improvement	Requirement for genetic correction; Risk of tumor generation

Pharmacological approaches to muscle regeneration have traditionally focused upon the delivery of anti-inflammatory drugs, steroids, hormones, and growth factors, for example. These approaches may hold promise in reverting the functional decline of sarcopenia or improving outcomes, but they do not specifically target myogenesis or directly affect the restoration tissue function. There is evidence that changing the environment of aged myogenic progenitor cells can promote skeletal muscle regeneration. Moreover, clinical evidence indicates that mother nature's ideal microenvironment, healthy ECM in the form of a biologic scaffolds, promotes myogenesis in patients with volumetric muscle loss (Table 5) (20).

1.9. Prognosis

Due to the complex etiology of sarcopenia, finding an effective treatment will require a multidisciplinary approach. Ultimate goal should be to identify dietary and exercise strategies, lifestyle changes and treatments that can prevent or delay the onset of sarcopenia (5).

Identification of the role of cytokines and small molecules, cellular metabolism, and endocrine-related changes have helped gain a better understanding of what causes sarcopenia and how it progresses. Regenerative medicine strategies, such as the use of an acellular, inductive approach that tailors the microenvironment and considers the many cell types involved in efficient skeletal muscle regeneration, could provide a promising alternative to traditional therapies including stem cell delivery, pharmacological treatment and physical rehabilitation. Combining these approaches might help in providing us with improved prognosis and better outcomes in patients with age-related muscle loss (20).

2. OBJECTIVES

The aim of this study was to translate the SarQoL® into Croatian language and develop a sarcopenia-specific quality of life questionnaire (SarQoL, Sarcopenia Quality of Life) designed for community-dwelling elderly subjects aged 65 years and older. Also, after succeeding in translating this questionnaire, we will present the results that we got through seven domains, finally proving our hypothesis that sarcopenia in elderly people indeed does reduce the quality of life.

3. MATERIALS AND METHODS

3.1. Research definition

According to its specific structure, this is a cross sectional type of research, which is also one of those included in the category of observational researches.

3.2. Participants

We used the definition of the European Working Group on Sarcopenia in Older People (EWGSOP) as criteria for diagnosing sarcopenic subjects. Subjects, aged 65 years and older, were recruited in an outpatient clinic in the University Hospital of Split. In total 51 patient participated in our research by filling out the given Croatian version of SarQoL questionnaire without any difficulties in understanding the given questionnaire.

Sarcopenia was defined as follows:
– An appendicular lean muscle mass/height2 (SMI) <5.5 kg/m2 for women and <7.26 kg/m2 for men assessed by Dual-energy X-ray absorptiometry.
– A muscle strength <20 kg for women and <30 kg for men assessed by a hydraulic hand dynamometer OR physical performance: ≤8 points for the Short Physical Performance Battery (SPPB) test.

Inclusion criteria included age ≥65 years and Croatian maternal language. Exclusion criteria were amputated limb and BMI above 30 kg/m2.

3.3. Research venue

The research took place in the Department of Immunology and Rheumatology of the Clinic for Internal diseases in the University Hospital of Split.

3.4. Methods of acquiring and processing data

For acquiring the neccessary data, I first performed a thorough and careful translation of the official SarQoL questionnaire in English language into Croatian language. This first version of the questionnaire was submitted to a Croatian linguist to ensure that it was free of any spelling or linguistic errors.

This questionnaire includes 55 items translated into 22 questions rated on a 4-point Likert scale. In view of observing the participants filling out the materials, the SarQoL was easy to complete, independently, in 10 min.

These 55 items that composed the SarQoL questionnaire were allocated to their respected domains. In total 7 domains were formed. The domains are the following ones: Physical and mental health, Locomotion, Body composition, Functionality, Activities of daily living, Leisure activities and Fears. Along with every patient's filled questionnaire, we also marked gender and age of each one of them, for later comparative purposes.

All of the data was later on inserted into the Microsoft Excel Programme, where it was sorted out as a table, with all the data being ready for use and interpretation of the upcoming results.

3.5. Statistical Analysis

In the empirical part of this thesis, by using quantitative methods, the quality of life in examined patients with a diagnosis of sarcopenia was tested. Data was collected by undertaking the SarQoL survey questionnaire among patients aged older than 65 years with a diagnosis of sarcopenia. By using chosen statements, a quality of life scale was formed. The scale ranges from 0 to 100, in which the value of 0 presents complete nonfunctionality, while the value of 100 presents a full funcionality of a healthy person. We used methods of graphical and table presentations, t-test, chi-square test, Wilcoxon's test for one independent sample and also correlational analysis. The distribution normality was tested by Kolmogorov-Smirnov test. Analysis was performed in statistical programme STATISTICA 12 (Licensed by University of Osijek). Conclusions were brought with a significance level of 5% . Testing of differences between the quality of life domains amongst male and female patients is tested with Mann-Whitney U test.

3.6. Ethical Approval

The Ethical Committe of the University Hospital of Split gave the approval for conducting this research.

4. RESULTS

Table 6. Gender and age of study participants

	F	**M**	**P**
Gender n (%)	30 (58.8)	21 (41.2)	0.208*
Age average (SD)	70.4 (3.1)	70.7 (3.4)	0.734 †

* chi square test
† t-test

Among the 51 patient, that participated in this research, there were 9 female patients more than male patients. Chi square test did not show any differences in prevalence according to gender (p=0.208).

Female gender patients in the sample are in average for 0.3 years (quartal) younger in compare to the patients of male gender. Testing has not confirmed any stastically significant difference (p=0.734) (Table 6).

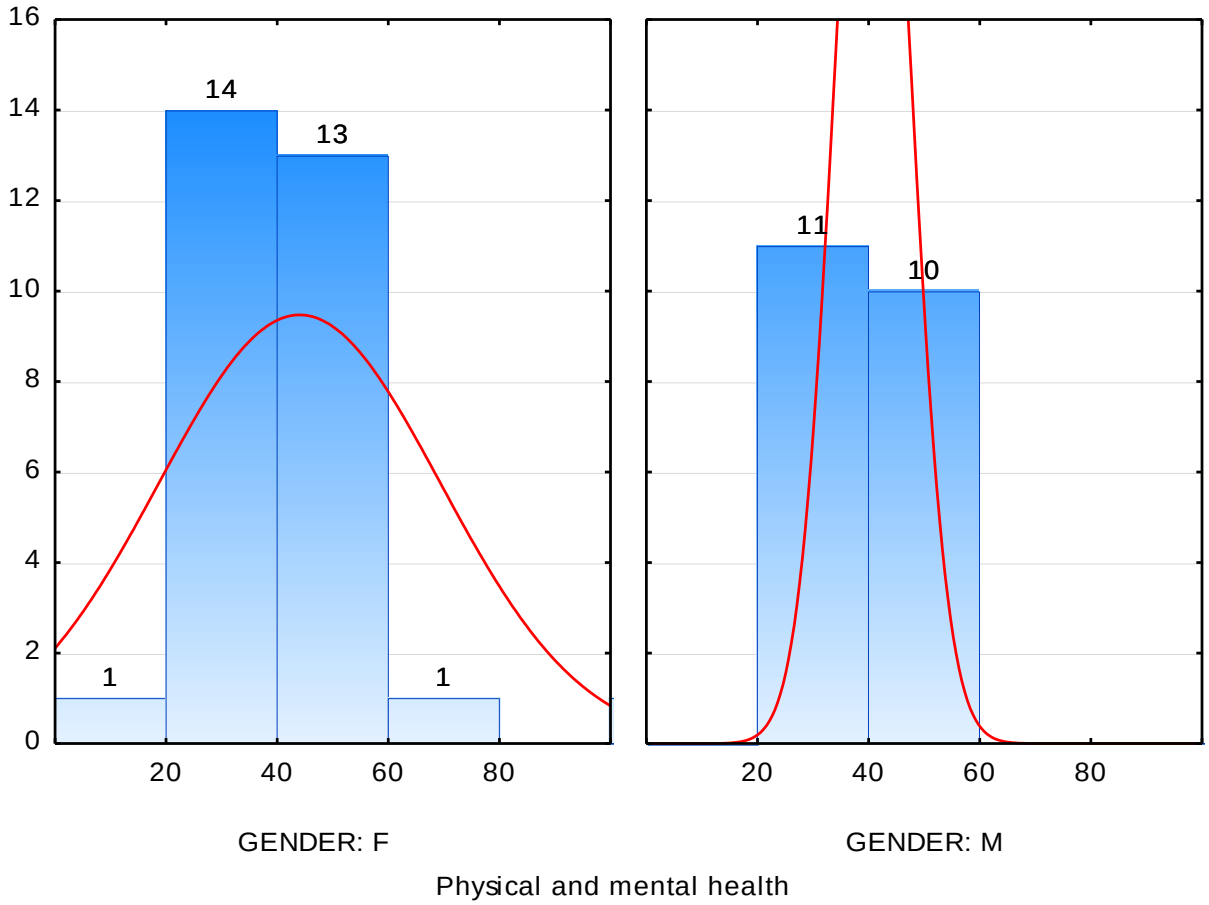

Figure 1. Physical and mental health domain among female and male participants (0-100)

The Physical and mental health domain among the examined female participants varied in a range from 0 to 80, while amongst male participants it varied in a range between 20 to 60. In both gender groups, the highest number of participants appeared in the range from 20 to 40. Results showed 14 female and 11 male participants in this range (Figure 1).

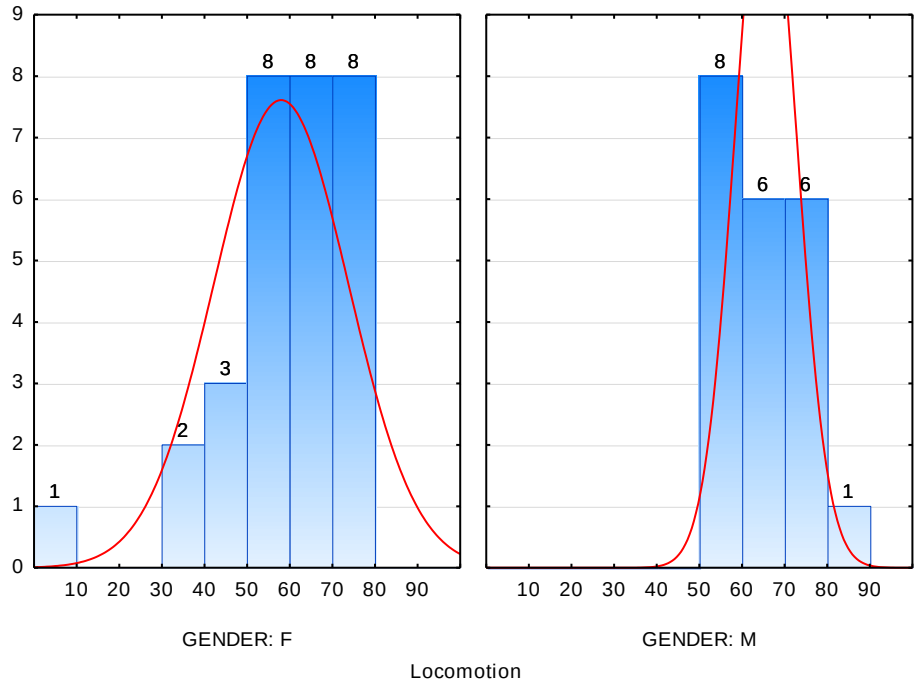

Figure 2. Locomotion domain among female and male participants (0-100)

Locomotion among examined female patients varied from 0 to 80, and most appeared in the range from 50 to 80. While among male patients it varied in a range from 50 to 90, with most appearing in the range from 50 to 60 (Figure 2).

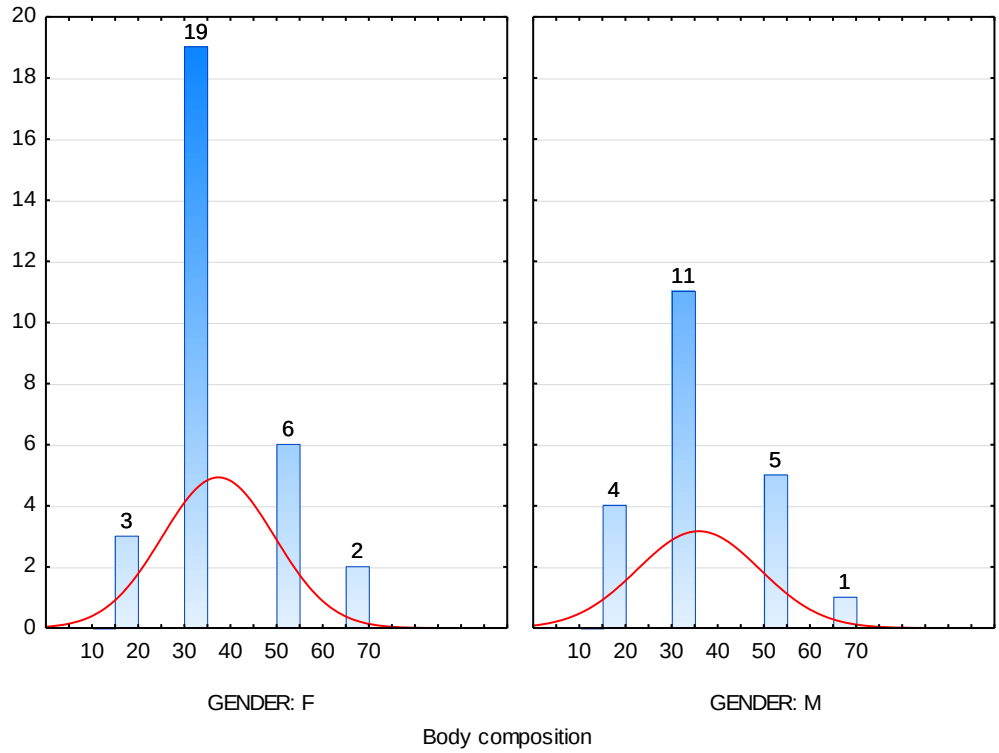

Figure 3. Body composition domain among female and male participants (0-100)

Body composition among the largest number of examined participants of both genders varied from 30 to 40. Results showed 19 female and 11 male participants presenting with this range (Figure 3).

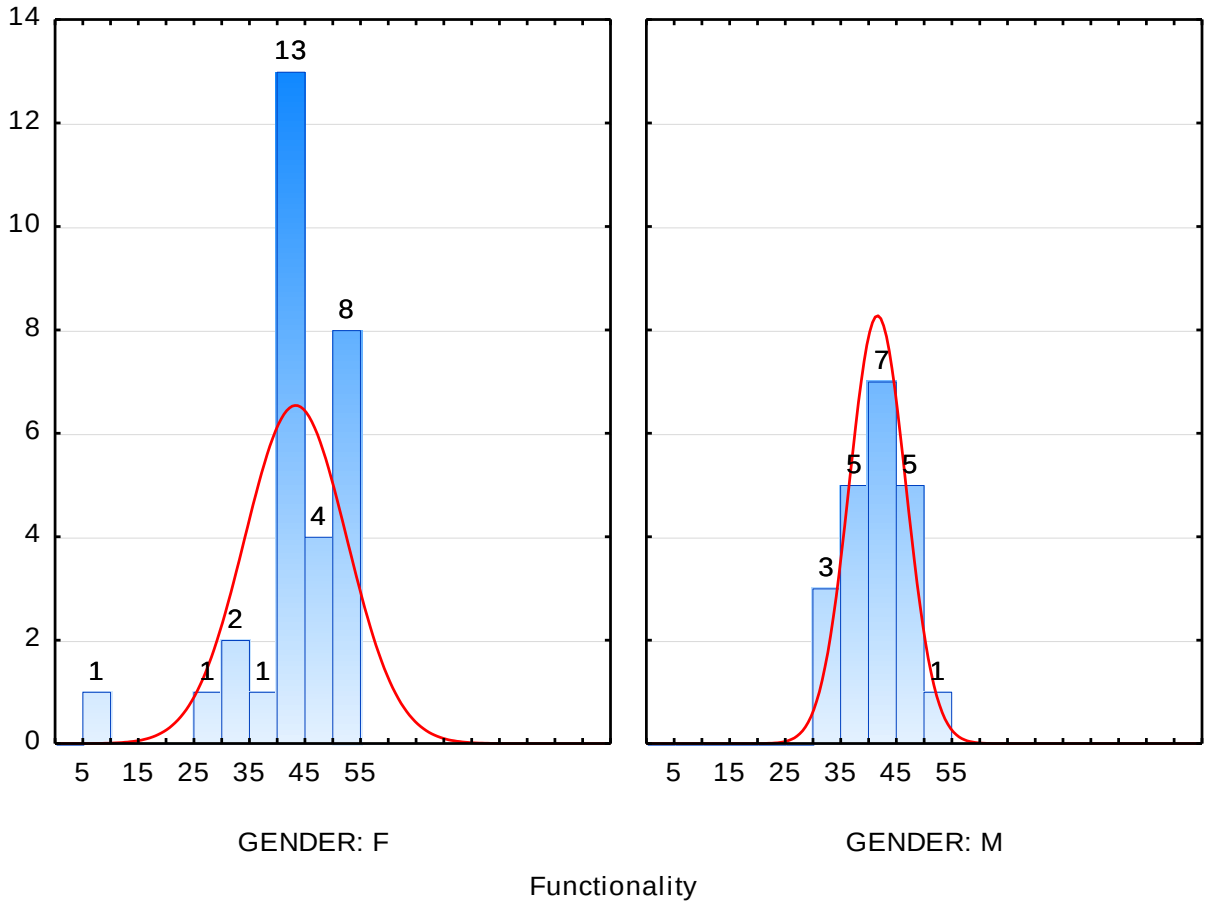

Figure 4. Functionality among female and male participants (0-100)

Functionality among female patients varied in a range of 5 to 55, while among the male patients it varied in a range of 30 to 55. Results showed that most of the female and male participants appear to be in the range of 40 to 45 (Figure 4).

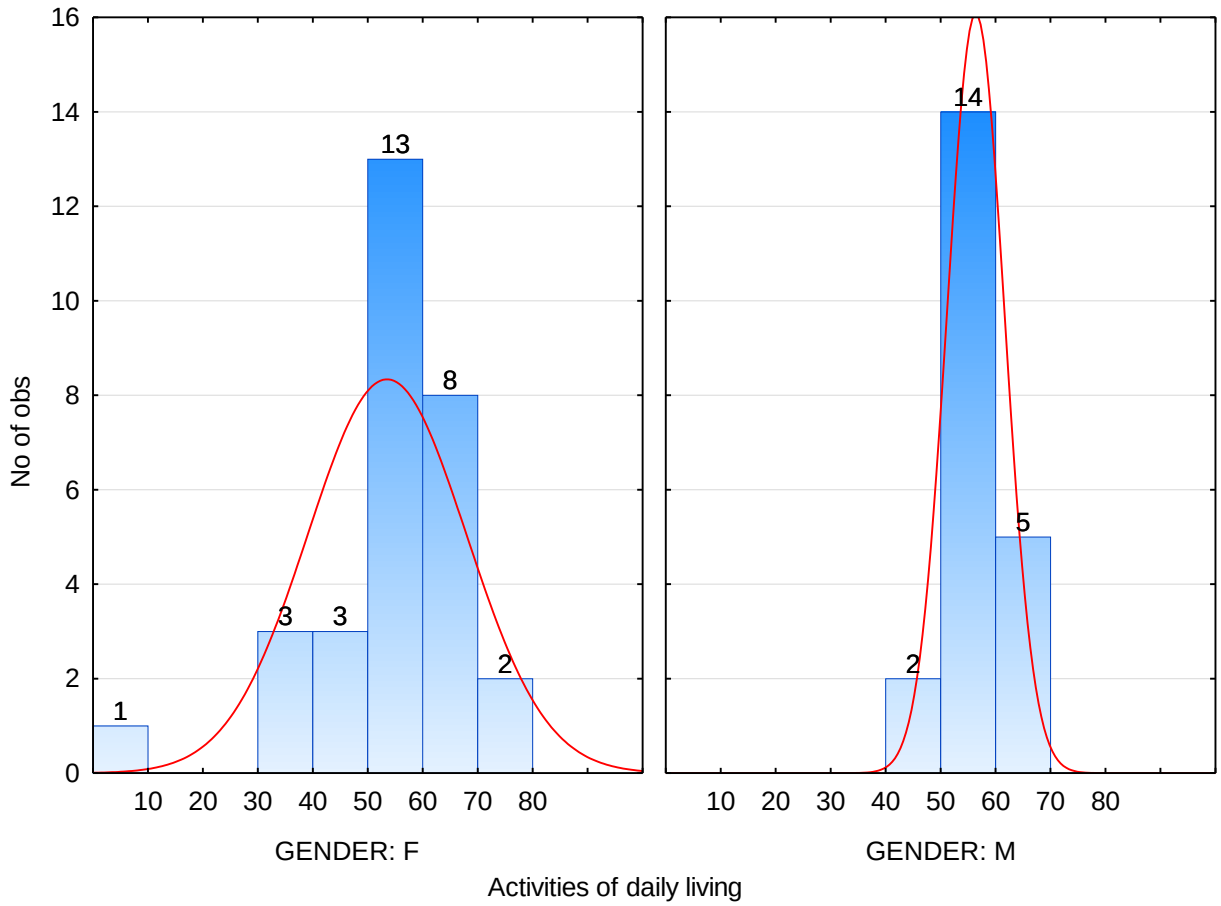

Figure 5. Activities of daily living among female and male participants (0-100)

Activites of daily living among observed female patients varied in a range of 0 to 80, while among observed male patients it varied in a range from 40 to 70. Most female participants presented in the range of 50 to 60. Also, most male participants presented in the range of 50 to 60 (Figure 5).

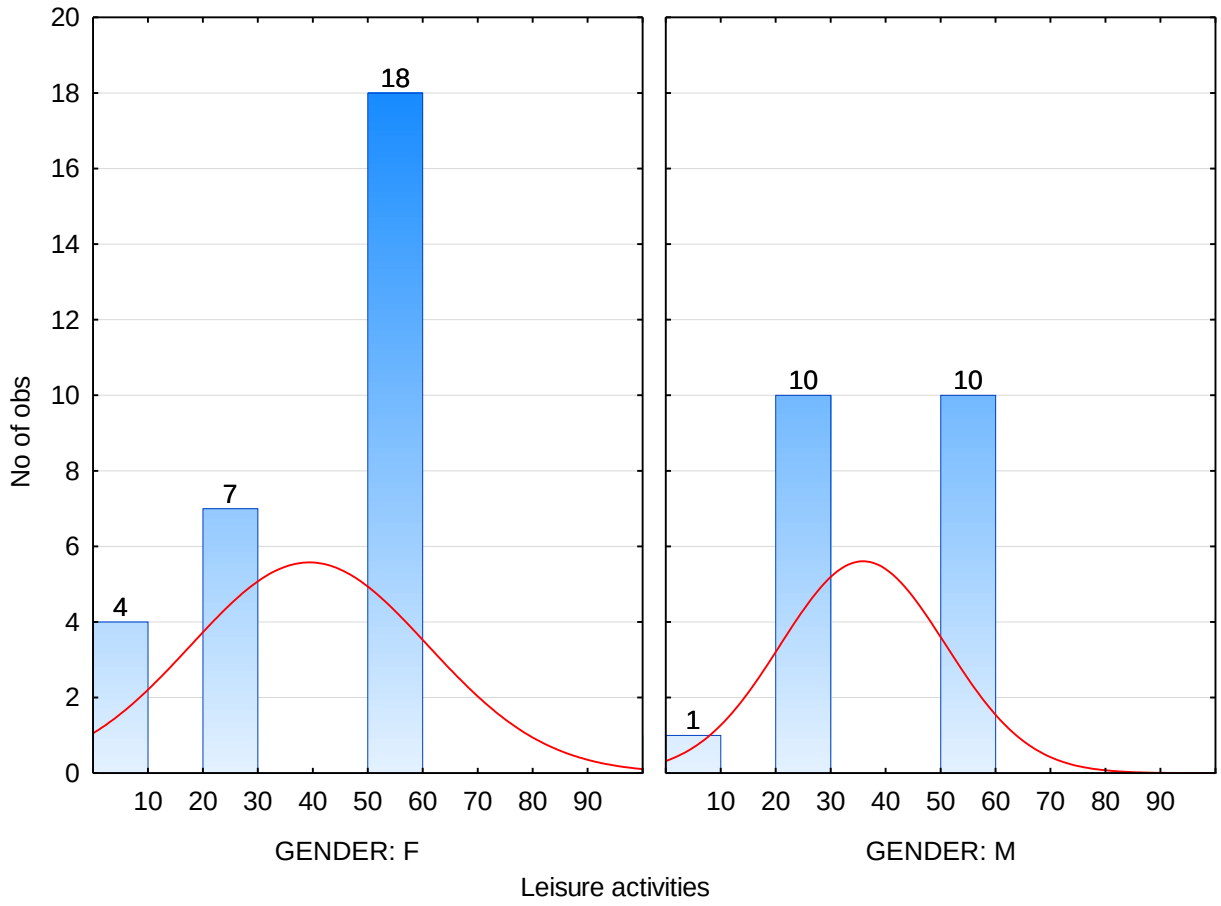

Figure 6. Leisure activities domain among female and male participants (0-100)

Leisure activites in both genders varied in a range of 0 to 60. Most of the female participants appeared to be in a range from 50 to 60, while most male participants appeared to be in ranges from 20 to 30 and from 50 to 60 (Figure 6).

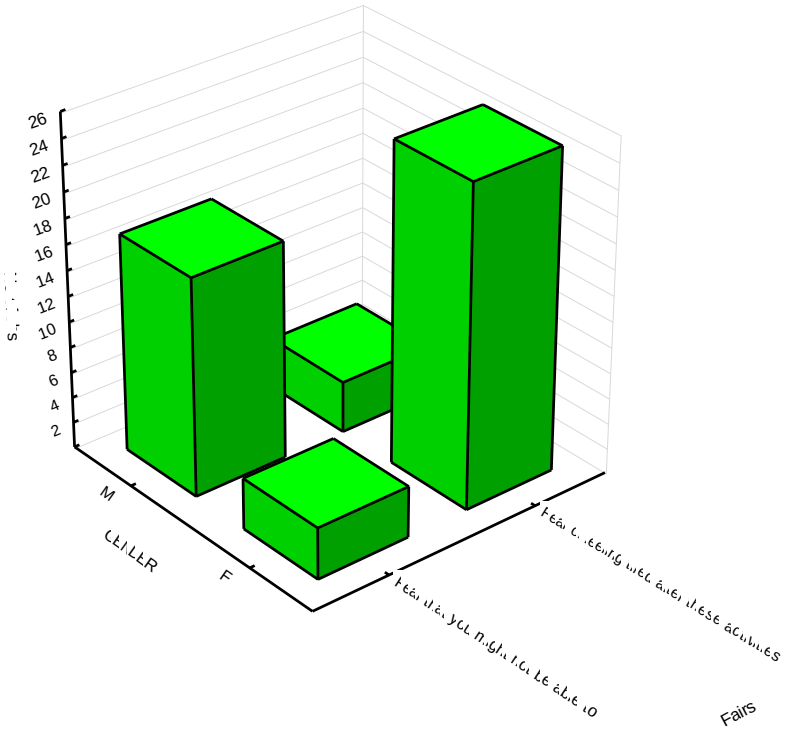

Figure 7. Fear domain among female and male participants (0-100)

We counted a number of 17 male patients saying that they had fear, that due to their current status, they would not be able to do certain activities, while on the other side 25 female patients admited to have fear of being tired after performing activities (Figure 7).

Table 8. Correlation between Quality of Life Domains amongst female participants

	Physical and mental health	Locomotion	Body composition	Functionality	Activities of daily living	Leisure activities	Fears
Physical and mental health	1						
	p= ---						
Locomotion	0.28	1					
	p=.070	p= ---					
Body composition	-0.02	0.31	1				
	p=.465	p=.050	p= ---				
Functionality	0.24	0.49	0.05	1			
	p=.105	p=.004	p=.399	p= ---			
Activities of daily living	0.33	0.86	0.10	0.49	1		
	p=.043	p=.000	p=.624	p=.004	p= ---		
Leisure activities	0.25	0.66	0.29	0.46	0.70	1	
	p=.095	p=.000	p=.065	p=.006	p=.000	p= ---	
Fears	-0.07	-0.47	-0.16	-0.56	-0.49	-0.54	1
	p=.367	p=.005	p=.204	p=.001	p=.004	p=.001	p= ---

It has been established that there is an existence of correlation amongst the statements (where the empirical p-value does not go above 0.05). This is a case of positive correlation on all statements, except „Fears“, while negative correlation shows us that „fear of feeling tired after these activities“ will be substituted with „fear that you might not be able to (do some activity)“ outcome of quality of life (Table 8).

Table 9. Correlation between Quality of Life Domains amongst male participants

	Physical and mental health	Locomotion	Body composition	Functionality	Activities of daily living	Leisure activities	Fears
Physical and mental health	1						
	p= ---						
Locomotion	0.10	1					
	p=.210	p= ---					
Body composition	-0.09	0.17	1				
	p=.0.385	p=.246	p= ---				
Functionality	-0.25	0.21	-0.30	1			
	p=.141	p=.165	p=.092	p= ---			
Activities of daily living	-0.16	0.19	0.23	0.21	1		
	p=.255	p=.203	p=.156	p=.180	p= ---		
Leisure activities	0.12	0.02	-0.45	0.05	-0.10	1	
	p=.295	p=.146	p=.020	p=.414	p=.336	p= ---	
Fears	0.31	-0.16	-0.38	-0.03	-0.02	0.56	1
	p=.086	p=.242	p=.045	p=.456	p=.473	p=.004	p= ---

Correlation amongst Quality of Life domains in male participants showed us that positive correlation was established only for „Fears“ (Table 9).

Table 10. Results of domain testing and its differences in female and male participants

	F me(IQR) †	**P**	**M** me(IQR) †	**P**
Qualitiy of life				
Physical and mental health	41 (35.4-47.9)	<0.001*	40 (35.4 - 43.8)	<0.001*
Locomotion	63 (51.9-70.4)	0.001*	67 (59.3 - 70.4)	<0.001*
Body composition	34 (33.3-50.0)	0.001*	34 (33.3- 50.0)	0.003*
Functionality	44 (41.7-50.0)	<0.001*	41 (38.2 - 45.1)	<0.001*
Activities of daily living	57 (50.0-60.0)	0.033*	56 (52.2 -58.9)	<0.001*
Leisure activities	50 (25.0–50.0)	0.505*	25 (25.0-50.0)	0.031*
Fears				
That you might not be able to	4 (13.8)	<0.001	17 (81.0)	0.007
Of feeling tired after these activities	25 (86.2)		4 (19.0)	

* Wilcoxon's test for one independent sample
† Me(IQR) - median (IQR Q1 – Q3 ; interquartil)
F-female, M-male

After the performed testing, it has been established that there is a higher level of Locomotion ($p<0.001$) and a higher level of Activities of daily living ($p<0.001$) amongst female patients. Leasure activities has moderate quality ($p=0.505$), while Physical and mental health ($p<0.001$), Body composition ($p<0.001$), and Functionality ($p<0.001$) have a low level of development. The indicator of life quality, Fear, in the form of „Fear of feeling tired after

certain activities“ statement, is statistically by far most common among female patients (p<0.001) (Table 10).

Among male patients, there is a high level of developed Locomotion (p<0.001) and Activities of daily living (p<0.001). Physical and mental health (p<0.001), Body composition (p=0.003), Functionality (p<0.001) and Leisure activities (p=0.031) are on a low level of development. The indicator of life quality, Fear, in the form of „that you might not be able to do“ statement is statistically ,with significance, most common among male patients (p=0.007) (Table 10).

Table 11. Differences between quality of life domains according to gender of participants

	F	**M**	**P**
Qualitiy of life			
Physical and mental health	41 (35.4-47.9)	40 (35.4 - 43.8)	0.923*
Locomotion	63 (51.9-70.4)	67 (59.3 - 70.4)	0.135*
Body composition	34 (33.3-50.0)	34 (33.3- 50.0)	0.713*
Functionality	44 (41.7-50.0)	41 (38.2 - 45.1)	0.054*
Activities of daily living	57 (50.0-60.0)	56 (52.2 -58.9)	0.871*
Leisure activities	50 (25.0–50.0)	25 (25.0-50.0)	0.421*
Fears			
Fear that you might not be able to	4 (13.8)	17 (81.0)	<0.001 †
Fear of feeling tired after these activities	25 (86.2)	4 (19.0)	

* Mann-Whitney U test
† chi square test

By testing the differences between the quality of life domains there has not been an established difference (p>0.05) for any of the indicators, except of Fear, where male patients were showed statistically more common with „Fear that you might not be able to“ , while female patients most commonly showed to have „Fear of feeling tired after these activities“ (p<0.001) (Table 11).

5. DISCUSSION

In the present study, we report the development of the first specific, self-administrated sarcopenia-related quality of life questionnaire, the SarQoL questionnaire. This questionnaire includes 55 items translated into 22 questions rated on a 4-point Likert scale. In view of the pretest, the SarQoL is easy to complete, independently, in around 10 minutes.

Sarcopenia is associated with the development of physical disability, with nursing home admission, depression, hospitalisation, many co-morbidities, poor physical performance, functional decline, falls and with short- and long-term mortality in hospitalised patients (25).

In 2012, Kull *et al.* (26) found a reduced quality of life in two domains (i.e. physical function and vitality) of the SF-36 questionnaire in sarcopenic subjects. Two other studies found that sarcopenic subjects presented poorer general health and physical functioning scores (27) and presented significantly more problems of mobility, self-care, usual activity and anxiety than non-sarcopenic subjects (28). Other studies showed an indirect association between sarcopenia and quality of life with a significant correlation between reduced grip strength, one of the components of sarcopenia, and reduced quality of life in the domains of physical functioning and general health (29).

After the performed testing in our research it has been established,and presented in Table 10, that there is a higher level of Locomotion ($p<0.001$) and a higher level of Activities of daily living ($p<0.001$) amongst female patients. Leasure activities has moderate quality ($p=0.505$), while Physical and mental health ($p<0.001$), Body composition ($p<0.001$), and Functionality ($p<0.001$) have a low level of development.
The indicator of life quality, Fear, in the form of „Fear of feeling tired after certain activities“ statement, is statistically by far most common among female patients ($p<0.001$), showing us that sarcopenia aside of impacting every day life activities, can also impact ones mental status, causing fears.

Among male patients, there is a high level of developed Locomotion ($p<0.001$) and Activities of daily living ($p<0.001$). Physical and mental health ($p<0.001$), Body composition ($p=0.003$), Functionality ($p<0.001$) and Leisure activities ($p=0.031$) are on a low level of development. The indicator of life quality, Fear, in the form of „that you might not be able to do“ statement is statistically ,with significance, most common among male patients

(p=0.007), showing us that males, as well as females, also encounter certain impacts on their mental status.

Such a tool, like this questionnaire, could enhance the accuracy of assessments of well-being and physical function, psychological and social implications of sarcopenic subjects. With the future expected development of interventions targeting sarcopenia, this tool will also be useful to measure the effectiveness and relevance of these new therapeutic strategies.

However, for an even more precise analysis, we did encounter certain limitations. In compare to some more detailed researches, such as the one Beaudart *et al.* did in 2016, we see that they used a much larger pool of participants, in compare to our 51 patient, which could have been limiting perhaps in some manner. And along with that, they included sarcopenic as well as non-sarcopenic participants. They compared the score of the SarQoL® between sarcopenic and non-sarcopenic subjects using a logistic regression after adjustment for potential confounding variables. Internal consistency reliability was determined using Cronbach's alpha coefficient; construct validity was assessed using convergent and divergent validities. Test–retest reliability was verified after a two-week interval using the intra-class correlation coefficient (ICC). At last, floor and ceiling effects were also tested (25).

A total of 296 subjects with a median age of 73.3 (68.9–78.6) years were recruited for this study. Among them, 43 were diagnosed sarcopenic. After adjustment for potential confounding factors, the total score and the scores of the different dimensions of the SarQoL® questionnaire were significantly lower for sarcopenic than for non-sarcopenic subjects (54.7 (45.9–66.3) for sarcopenic vs. 67.8 (57.3 – 79.0) for non sarcopenic, OR 0.93 (95%CI 0.90–0.96)). Regarding internal consistency, the Cronbach's alpha coefficient was 0.87 (29). The SarQoL® questionnaire was shown to be valid, consistent, and reliable and can therefore be recommended for clinical and research purposes. However, its sensitivity to change needs to be assessed in future longitudinal studies (25).

The SarQoL has been shown to be comprehensible by the target population in our research. Investigations are now required to test the psychometric properties of this questionnaire in the future.

6. CONCLUSION

1. The SarQoL questionnaire was translated successfully, and was understood and solved by patients without difficulties.

2. The obtained results showed us that sarcopenia decreases the quality of life and causes difficulties in every day life for patients that are diagnosed with sarcopenia.

3. Along with causing difficulties in every day activities, it has also been noticed that all patients with sarcopenia, that participated in this research, experienced also some form of fear.

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8. SUMMARY

Objectives: The aim of this study was to translate the official Sarcopenia Quality of Life questionnaire into Croatian language so that it is understandable for patients to answer it, after which we obtained the answers to assess further on how sarcopenia affects their lives through 7 different domains.

Materials and methods: The translated SarQoL questionnaire was given to 51 patient, all of whom were older than 65 and had a diagnosis of sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOP). Diagnoses were verified by medical record review collected from archives of the Department of Clinical Immunology and Rheumatology, University Hospital Split.

Results: After the performed testing it has been established that there is a higher level of „Locomotion“ ($p<0.001$) and a higher level of „Daily living activities“ ($p<0.001$) amongst female patients. „Leisure activities“ has moderate quality ($p=0.505$), while „Physical and mental health“ ($p<0.001$), „Body composition“ ($p<0.001$), and „Functionality“ ($p<0.001$) have a low level of development. On the other hand, among male patients, there is a high level of developed „Locomotion“ ($p<0.001$) and „Daily living activities“ ($p<0.001$). However, „Physical and mental health“ ($p<0.001$), „Body composition“ ($p=0.003$), „Functionality“ ($p<0.001$) and „Leisure activities“ ($p=0.031$) are on a low level of development. Male patients were showed statistically more common with „Fear that you might not be able to“ , while female patients most commonly showed to have „Fear of feeling tired after these activities“ ($p<0.001$).

Conclusions: The SarQoL questionnaire was translated successfully, and was understood and solved by patients without difficulties. The obtained results showed us that sarcopenia indeed decreases and causes difficulties in the quality of every day life for patients that are diagnosed with sarcopenia.

9. CROATIAN SUMMARY

Naslov: Prijevod i validacija Upitnika o kvaliteti života kod ljudi sa sarkopenijom

Ciljevi: Prevesti službeni SarQoL upitnik na hrvatski jezik kako bi bio razumljiv za pacijente koji ga ispunjavaju u svrhu istraživanja, a nakon čega ćemo iskoristiti dobivene odgovore te ih provesti kroz 7 domena kako bi ustvrdili kako sarkopenija utječe na kvalitetu života.

Materijali i metode: U ispunjavanju prevedenoga SarQoL upitnika je sudjelovao 51 pacijent, koji je imao/la najmanje 65 godina te koji je imao/la dijagnozu sarkopenije prema pravilima koje nalaže Europska radna skupina za sarkopeniju kod osoba starije dobi (EWGSOP). Dijagnoze sarkopenije su ovjerene provjerom medicinskih zapisa iz arhive Odjela kliničke imunologije i reumatologije, KBC Split.

Rezultati: Nakon provedenog testiranja utvrđeno je da među pacijenticama postoji viša razina lokomotornosti ($p<0,001$) i aktivnosti dnevnog življenja ($p<0,001$). Ležerna aktivnost je umjereno kvalitetna ($p=0,505$), dok je fizičko i mentalno zdravlje ($p<0,001$), sastav tijela ($p<0,001$), te funkcionalnost ($p<0,001$) na niskoj razini razvijenosti. Među muškim pacijentima postoji visoka razina razvijenosti lokomotornosti ($p<0,001$), te aktivnosti dnevnog življenja ($p<0,001$). Ipak, fizičko i mentalno zdravlje ($p<0,001$), sastav tijela ($p=0,003$), funkcionalnost ($p<0,001$) i ležerne aktivnosti ($p=0,031$) su na niskoj razini razvijenosti. Statistički su muški pacijenti izrazili strah najčešće pod izjavom "Imam strah kako neću moći izvršiti neku radnju", dok su pacijentice najčešće birale tvrdnju "Strah me osjećaja umora nakon obavljanja tih navedenih radnji".

Zaključci: SarQoL upitnik je uspješno preveden te je bio razumljiv i rješen bez ikakvih problema od strane pacijenata koji su sudjelovali. Dobiveni rezultati su nam pokazali kako sarkopenija uistinu stvara poteškoće i umanjuje kvalitetu svakodnevnog života pacijentima koji su dijagnosticirani sa sarkopenijom.

10. CURRICULUM VITAE

PERSONAL DATA

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EDUCATION

2000-2004 – O.Š. "Pojišan"

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KNOWLEDGE AND SKILLS

Active usage of English language (CAE ,Cambridge Advanced Exam Test, C1 level)

Active usage of German language

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OTHER ACTIVITIES

- 16.8. – 31.8.2014 – famulatur (medical clerkship) in St.Agnes-Hospital in Bocholt, Germany (departments of Emergency Medicine and Radiology)

- Co-founder and vice-president of ISA USSM (International Students Association of University of Split School of Medicine)